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An Expedient Synthesis of Oxindole Dimers by Direct Oxidative Dimerization of Oxindoles

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Oxindole dimers have been used as intermediates in the synthesis of various cyclotryptamine alkaloids. An efficient direct synthesis of oxindole dimers has been carried out from 3-substituted oxindoles *via* an oxidative dimerization using manganese(III) acetate or copper acetate/silver acetate system.

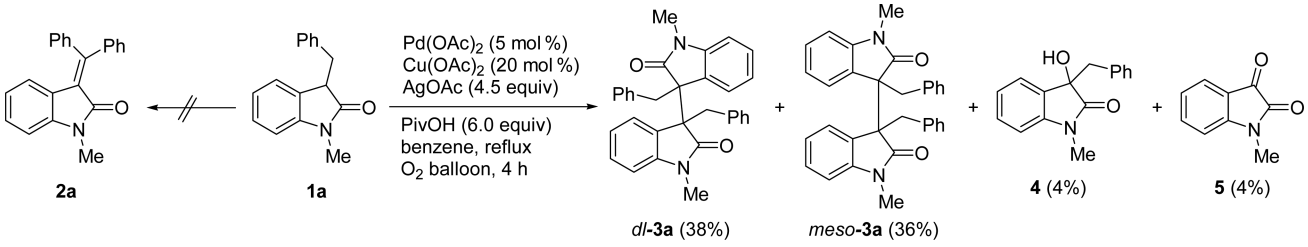
Key Words : Oxindole dimers, Oxidative dimerization, Manganese(III) acetate, Oxindoles

Introduction

Oxindole dimers have been used as intermediates in the synthesis of various cyclotryptamine alkaloids.[1] Thus, extensive studies have been carried out for the preparation of oxindole dimers.[2,3] Rodrigo and co-workers reported a dimerization of oxindole anion with carbon tetraiodide *via* a radical anion chain mechanism.[2a] Inada and Morita reported an oxindole demerization using cobalt(II) Schiff's base complexes.[2b] Some indirect synthesis of oxindole dimers have also been reported.[3]

Results and Discussion

Recently, we reported a palladium-catalyzed arylation reaction of alkylidene oxindoles.[4] During the studies, we examined a feasibility for the palladium-catalyzed dehydrogenation/oxidative arylation reaction[5] of oxindole **1a** to **2a**, as shown in Scheme 1. In the reaction, however, we did not observe the formation of **2a** in any trace amount. Instead, an oxindole dimer **3a** was obtained in good yield (74%) along with trace amounts of 3-hydroxyoxindole **4** (4%) and isatin **5** (4%). We were interested in the high-yield formation of



Scheme 1

Table 1. Optimization of oxidative dimerization of **1a** to **3a**

Entry	Conditions	*dl* (%)/*meso* (%)[a]	**1a** (%)[a]
1	$Cu(OAc)_2$ (20 mol %), AgOAc (4.5 equiv), benzene, O_2, reflux, 4 h	40 / 38	0
2	AgOAc (4.5 equiv), benzene, O_2, reflux, 12 h	0 / 0	98
3	$Cu(OAc)_2$ (20 mol %), benzene, O_2, reflux, 36 h	< 5 / < 5	85
4	$Cu(OAc)_2$ (2.2 equiv), benzene, O_2, reflux, 72 h	32 / 31	26
5	$Cu(OAc)_2$ (20 mol %), AgOAc (2.0 equiv), benzene, O_2, reflux, 24 h	43 / 39	0
6	$Cu(OAc)_2$ (20 mol %), AgOAc (2.0 equiv), benzene, N_2, reflux, 36 h	46 / 42	0
7	$Cu(OAc)_2$ (20 mol %), $K_2S_2O_8$ (2.0 equiv), benzene, N_2, reflux, 48 h	36 / 35	9
8	$Mn(OAc)_3$ (2.0 equiv), benzene, N_2, reflux, 4 h	46 / 44	0
9	$Mn(OAc)_3$ (1.1 equiv), benzene, N_2, reflux, 12 h	42 / 40	6
10	$Ce(NH_4)_2(NO_3)_6$ (2.0 equiv), benzene, N_2, reflux, 4 h	10 / 9	9[b]
11	$FeCl_3$ (2.0 equiv), benzene, N_2, reflux, 15 h	9 / 8	60
12	$K_3Fe(CN)_6$ (2.0 equiv), benzene, N_2, reflux, 36 h	32 / 34	14

[a]Isolated yield. [b]*N*-Methylisatin (**5**) was isolated in an appreciable amount (37%).

oxindole dimers.

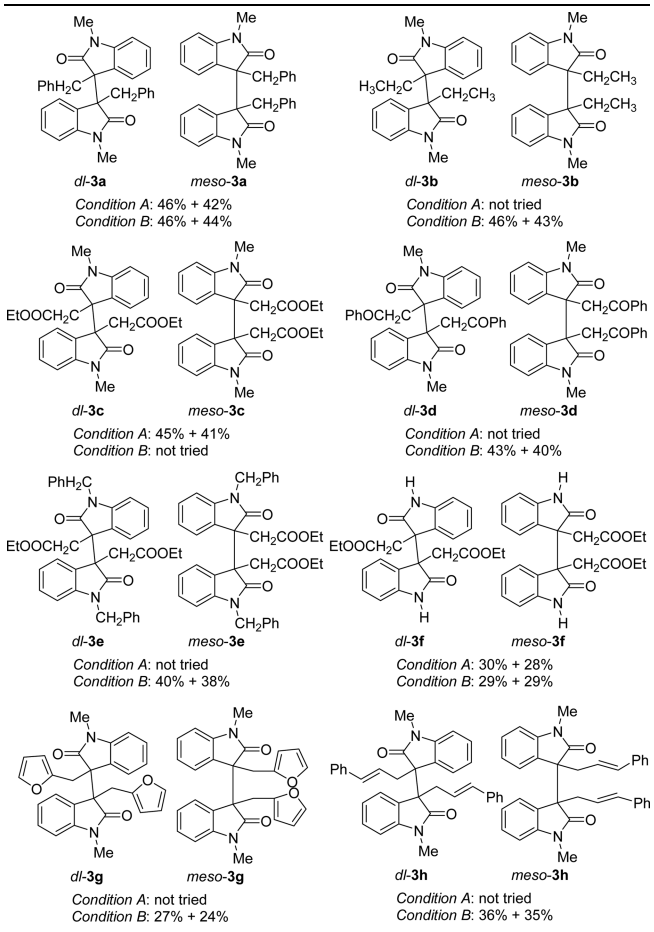
In the reaction shown in Scheme 1, the role of a palladium catalyst and pivalic acid was unclear. Thus we examined the reaction conditions in detail, and the results are summarized in Table 1. The reaction without $Pd(OAc)_2$ and PivOH afforded **3a** in a similar yield (entry 1), as expected. However, the reaction with only AgOAc did not produce **3a** (entry 2). The reaction in the presence of a catalytic amount of $Cu(OAc)_2$ afforded **3a** in only a trace amount (entry 3). When we used 2.2 equiv of $Cu(OAc)_2$, **3a** was isolated in moderate yield (entry 4).[6] Reducing the amount of an expensive AgOAc to 2.0 equiv gave a similar yield (82%); however, somewhat longer reaction time (24 h) was required (entry 5). The reaction under N_2 balloon atmosphere showed more clean reaction (entry 6), and actually **3a** was obtained in an increased yield (88%). The use of $K_2S_2O_8$ instead of AgOAc was less effective (entry 7). Based on the papers dealing with an oxidative dimerization,[6-8] we examined other dimerization conditions (entries 8-12). The use of $Mn(OAc)_3$ showed an excellent result (entry 8), and **3a** was isolated in high yield (90%). When we used 1.1 equiv of $Mn(OAc)_3$, the reaction was not completed even after 12 h (entry 9). The use of cerium(IV) ammonium nitrate (entry 10),[8e] $FeCl_3$ (entry 11),[2b] and potassium ferricyanide (entry 12)[2b,8a] were less effective. Based on the experimental results, we selected the conditions of entry 6 (*condition A*) and 8 (*condition B*) as optimum conditions.

The oxindole dimer **3a** was formed as a mixture of *dl*- and *meso*-diastereoisomers.[2a] The ratio of *dl*/*meso* was almost equal throughout the whole entries in Table 1. A *dl*-isomer **3a** appeared on TLC at higher R_f value than the corresponding *meso*-**3a**, presumably because the dipole moment of *dl*-**3a** is smaller than the *meso*-**3a**.[2a] In their ^{1}H NMR spectra, the benzyl moieties appeared as typical AB quartets. The benzyl protons of *dl*-**3a** appeared slightly downfield (*ca.* 0.2 ppm) than those of the *meso*-**3a**.[2a]

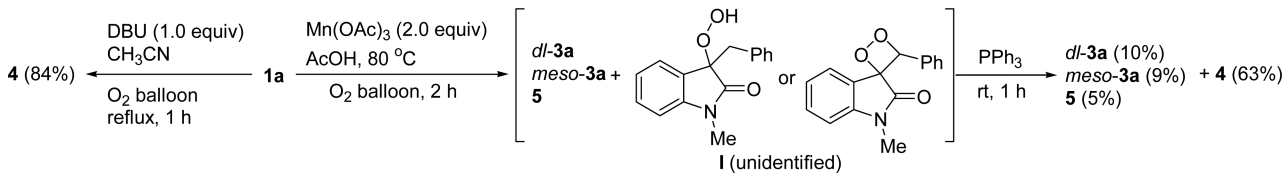
In order to examine the generality of the oxidative dimerization, various 3-substituted oxindoles **1b-h** were prepared according to the reported methods.[3d,4,9] The reactions of **1b-h** were examined under the optimized *conditions A* and/or *B*, and the results are summarized in Table 2. The dimerizations with various 3-substituted oxindoles **1b-h** afforded the corresponding oxindole dimers **3b-h** in good yields (51-89%). In all entries, *dl*- and *meso*-diastereoisomers were formed in almost equal amounts irrespective of the C3- and *N*-substituents.

The oxindole dimers **3** might be formed by dimerization of an oxindole radical which could be produced from **1** by the action of $Mn(OAc)_3$[7] or $Cu(OAc)_2$.[2a,3d] The side product **4** must be formed *via* an aerobic oxidation of **1a** with molecular oxygen;[2b,3d] however, the mechanism for the formation of **5** is unclear at this stage.[2b] The amounts of **4** and **5** increased under O_2 atmosphere, although a trace amount of **4** and **5** was observed even under N_2 balloon atmosphere, presumably due to the presence of a trace amount of molecular oxygen in the reaction flask. As shown in Scheme 2, the reaction of **1a** was examined in AcOH in the presence of $Mn(OAc)_3$ under O_2 balloon atmosphere. The starting material **1a** disappeared completely after 2 h, and small amounts of *dl*-**3a**, *meso*-**3a** and **5** were observed along with unknown compound **I** as a major component on TLC. We assumed that compound **I** might be a hydroperoxide intermediate,[3d] which could be formed from oxindole radical and molecular oxygen. As expected, a treatment of the reaction mixture with PPh_3 afforded **4** as a major product (63%). Compound **4**

Table 2. Synthesis of oxindole dimers **3a-h**[a]



[a]Condition A: $Cu(OAc)_2$ (20 mol %), AgOAc (2.0 equiv), benzene, reflux, 36 h. Condition B: $Mn(OAc)_3$ (2.0 equiv), benzene, reflux, 4 h.



Scheme 2

could also be prepared using DBU according to the reported method,[3d,10] as shown in Scheme 2.

In summary, we disclosed an efficient direct synthesis of oxindole dimers from 3-substituted oxindoles *via* an oxidative dimerization using manganese(III) acetate or copper acetate/silver acetate system.

Experimental Section

Preparation of Starting Materials. The starting materials **1a-h** were prepared according to the reported methods,[3d,4,9] from *N*-methyloxindole, isatin and *N*-substituted isatins. The spectroscopic data of unknown compound **1h** are as follows.

Compound 1h: Pale yellow solid, mp 60-62 °C; IR (KBr) 1710, 1613, 1469, 1348 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 2.50-2.64 (m, 1H), 2.88-3.00 (m, 1H), 3.13 (s, 3H), 3.44-3.54 (m, 1H), 6.04-6.18 (m, 1H), 6.38 (d, *J* = 15.9 Hz, 1H), 6.74 (d, *J* = 7.5 Hz, 1H), 6.95 (t, *J* = 7.5 Hz, 1H), 7.03-7.28 (m, 7H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 26.16, 34.31, 45.56, 107.97, 122.25, 124.21, 125.85, 126.16, 127.25, 127.98, 128.46, 128.57, 132.98, 137.14, 144.27, 177.07; ESIMS *m/z* 264 $[M+H]^+$.

Typical Procedure for the Synthesis of Dimer 3a. A mixture of **1a** (119 mg, 0.5 mmol) and $Mn(OAc)_3$ dihydrate (268 mg, 2.0 equiv) in benzene (2 mL) was heated to reflux for 4 h under N_2 balloon atmosphere. After the usual aqueous extractive workup and column chromatographic purification process (hexanes/CH_2Cl_2/ether, 10:3:1), *dl*-**3a** (55 mg, 46%) and *meso*-**3a** (52 mg, 44%) were obtained as pale yellow solids. Other compounds were synthesized similarly, and the spectroscopic data of **3a-h** are as follows.

***dl*-3a:** 46%; R_f = 0.51 (hexanes/ether, 1:3); pale yellow solid, mp 211-212 °C; IR (KBr) 1703, 1611, 1471, 1376 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 2.82 (s, 6H), 3.70 (d, *J* = 12.6 Hz, 2H), 4.24 (d, *J* = 12.6 Hz, 2H), 6.07 (d, *J* = 7.5 Hz, 2H), 6.68 (t, *J* = 7.5 Hz, 2H), 6.72-6.92 (m, 12H), 7.12 (d, *J* = 7.5 Hz, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 25.42, 35.28, 57.43, 107.10, 121.40, 123.86, 125.98, 127.23, 127.93, 128.17, 130.30, 135.97, 142.99, 176.94; ESIMS *m/z* 473 $[M+H]^+$. Anal. Calcd for $C_{32}H_{28}N_2O_2$: C, 81.33; H, 5.97; N, 5.93. Found: C, 81.14; H, 6.07; N, 5.78.

***meso*-3a:** 44%; R_f = 0.23 (hexanes/ether, 1:3); pale yellow solid, mp 221-222 °C; IR (KBr) 1703, 1609, 1471, 1375 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 2.60 (s, 6H), 3.42 (d, *J* = 12.6 Hz, 2H), 4.18 (d, *J* = 12.6 Hz, 2H), 6.34 (d, *J* = 7.8 Hz, 2H), 6.66-6.96 (m, 14H), 7.07 (t, *J* = 7.8 Hz, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 25.51, 36.82, 58.08, 107.72, 121.26, 124.56, 126.17, 127.20, 128.46, 128.51, 130.32, 135.35, 144.37, 175.88; ESIMS *m/z* 473 $[M+H]^+$. Anal. Calcd for $C_{32}H_{28}N_2O_2$: C, 81.33; H, 5.97; N, 5.93. Found: C, 81.41; H, 6.02; N, 5.66.

***dl*-3b:** 46%; R_f = 0.43 (hexanes/ether, 1:3); white solid, mp 231-232 °C; IR (KBr) 1704, 1609, 1493, 1355 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.33 (t, *J* = 7.5 Hz, 6H), 2.20-2.36 (m, 2H), 2.62-2.80 (m, 2H), 3.00 (s, 6H), 6.34 (d, *J* = 7.5 Hz, 2H), 6.75 (t, *J* = 7.5 Hz, 2H), 6.88-7.00 (m, 4H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 8.86, 21.42, 25.52, 57.39, 107.10, 121.55, 123.03, 127.90, 128.65, 143.52, 177.50; ESIMS *m/z* 349 $[M+H]^+$. Anal. Calcd for $C_{22}H_{24}N_2O_2$: C, 75.83; H, 6.94; N, 8.04. Found: C, 75.91; H, 7.10; N, 7.89.

***meso*-3b:** 43%; R_f = 0.14 (hexanes/ether, 1:3); white solid, mp 201-202 °C; IR (KBr) 1711, 1609, 1468, 1350 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.36 (t, *J* = 7.5 Hz, 6H), 1.94-2.12 (m, 2H), 2.60-2.78 (m, 2H), 2.88 (s, 6H), 6.47 (d, *J* = 7.8 Hz, 2H), 6.62 (d, *J* = 7.8 Hz, 2H), 6.78 (t, *J* = 7.8 Hz, 2H), 7.16 (t, *J* = 7.8 Hz, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 8.57, 22.94, 25.70, 57.85, 107.55, 121.37, 123.80, 128.31, 128.77, 144.79, 176.69; ESIMS *m/z* 349 $[M+H]^+$.

***dl*-3c:**[2a] 45%; R_f = 0.50 (hexanes/ether, 1:4); pale yellow solid, mp 191-192 °C; IR (KBr) 1737, 1711, 1612, 1471, 1376 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.83 (t, *J* = 6.9 Hz, 6H), 3.02 (s, 6H), 3.12 (d, *J* = 15.9 Hz, 2H), 3.60-3.82 (m, 4H), 3.96 (d, *J* = 15.9 Hz, 2H), 6.32 (d, *J* = 7.8 Hz, 2H), 6.74 (t, *J* = 7.8 Hz, 2H), 6.95 (t, *J* = 7.8 Hz, 2H), 6.96 (d, *J* = 7.8 Hz, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 13.72, 25.74, 33.92, 52.42, 60.33, 107.24, 121.37, 122.81, 126.82, 128.74, 143.83, 169.72, 176.57; ESIMS *m/z* 465 $[M+H]^+$.

***meso*-3c:**[2a] 41%; R_f = 0.23 (hexanes/ether, 1:4); pale yellow solid, mp 153-154 °C; IR (KBr) 1737, 1718, 1611, 1471, 1376 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.85 (t, *J* = 7.2 Hz, 6H), 2.89 (s, 6H), 3.06 (d, *J* = 16.2 Hz, 2H), 3.68 (d, *J* = 16.2 Hz, 2H), 3.60-3.84 (m, 4H), 6.46 (d, *J* = 7.5 Hz, 2H), 6.63 (d, *J* = 7.5 Hz, 2H), 6.77 (t, *J* = 7.5 Hz, 2H), 7.19 (t, *J* = 7.5 Hz, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 13.72, 25.99, 35.58, 53.13, 60.49, 107.88, 121.35, 123.44, 127.11, 129.15, 145.08, 169.30, 175.50; ESIMS *m/z* 465 $[M+H]^+$. Anal. Calcd for $C_{26}H_{28}N_2O_6$: C, 67.23; H, 6.08; N, 6.03. Found: C, 67.52; H, 6.34; N, 5.82.

***dl*-3d:** 43%; R_f = 0.43 (hexanes/ether, 1:4); pale yellow solid, mp 233-234 °C; IR (KBr) 1703, 1612, 1471, 1344 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 3.11 (s, 6H), 3.75 (d, *J* = 17.7 Hz, 2H), 5.03 (d, *J* = 17.7 Hz, 2H), 6.35 (d, *J* = 7.2 Hz, 2H), 6.65 (t, *J* = 7.2 Hz, 2H), 6.85 (d, *J* = 7.2 Hz, 2H), 6.92 (t, *J* = 7.2 Hz, 2H), 7.28-7.52 (m, 6H), 7.84 (d, *J* = 7.2 Hz, 4H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 25.89, 38.16, 52.69, 107.29, 121.17, 121.97, 127.35, 128.15, 128.47, 128.48, 133.26, 136.42, 144.03, 177.49, 196.45; ESIMS *m/z* 529 $[M+H]^+$.

***meso*-3d:** 40%; R_f = 0.16 (hexanes/ether, 1:4); pale yellow solid, mp 203-204 °C; IR (KBr) 1712, 1612, 1470, 1347 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 2.94 (s, 6H), 3.95 (d, *J* = 17.4 Hz, 2H), 4.52 (d, *J* = 17.4 Hz, 2H), 6.41 (br s, 2H), 6.69 (d, *J* = 7.8 Hz, 2H), 6.74 (t, *J* = 7.8 Hz, 2H), 7.19 (t, *J* = 7.8 Hz, 2H), 7.33 (t, *J* = 7.2 Hz, 4H), 7.46 (t, *J* = 7.2 Hz, 2H), 7.79 (d, *J* = 7.2 Hz, 4H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 26.10, 39.94, 53.32, 108.05, 121.07, 122.65, 127.95, 127.97, 128.47, 128.90, 133.21, 136.43, 145.40, 176.06, 195.48; ESIMS *m/z* 529 $[M+H]^+$. Anal. Calcd for $C_{34}H_{28}N_2O_4$: C, 77.25; H, 5.34; N, 5.30. Found: C, 77.29; H, 5.53; N, 5.24.

***dl*-3e:** 40%; R_f = 0.63 (hexanes/ether, 1:3); white solid, mp 150-152 °C; IR (KBr) 1736, 1709, 1612, 1467, 1368 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.74 (t, *J* = 7.2 Hz, 6H), 3.19 (d, *J* = 15.9 Hz, 2H), 3.54-3.84 (m, 4H), 4.05 (d, *J* = 15.9 Hz, 2H), 4.45 (d, *J* = 15.6 Hz, 2H), 4.99 (d, *J* = 15.6 Hz, 2H), 6.26 (d, *J* = 7.8 Hz, 2H), 6.57 (t, *J* = 7.8 Hz, 2H), 6.84 (t, *J* =

7.8 Hz, 2H), 6.94 (d, J = 7.8 Hz, 2H), 7.14-7.30 (m, 10H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 13.66, 34.50, 44.31, 52.33, 60.40, 108.45, 121.68, 123.55, 126.76, 127.47, 127.81, 128.55, 128.57, 135.42, 143.41, 169.61, 176.90; ESIMS *m/z* 617 $[M+H]^+$. Anal. Calcd for $C_{38}H_{36}N_2O_6$: C, 74.01; H, 5.88; N, 4.54. Found: C, 74.35; H, 5.93; N, 4.48.

***meso*-3e:** 38%; R_f = 0.49 (hexanes/ether, 1:3); white solid, mp 84-86 °C; IR (KBr) 1735, 1721, 1610, 1467, 1367 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.81 (t, J = 7.2 Hz, 6H), 3.17 (d, J = 15.9 Hz, 2H), 3.72 (d, J = 15.9 Hz, 2H), 3.55-3.60 (m, 4H), 4.54 (d, J = 15.9 Hz, 2H), 4.85 (d, J = 15.9 Hz, 2H), 6.46 (d, J = 7.5 Hz, 2H), 6.73 (br s, 2H), 6.86-7.26 (m, 14H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 13.75, 36.46, 44.58, 52.94, 60.60, 109.33, 121.73, 123.72, 127.11, 127.25, 128.48 (2C), 129.14, 135.71, 144.73, 169.23, 176.08; ESIMS *m/z* 617 $[M+H]^+$.

***dl*-3f:** 29%; R_f = 0.44 (CH_2Cl_2/MeOH, 19:1); white solid, mp 241-242 °C; IR (KBr) 3283, 1732, 1620, 1473, 1373 cm^{-1}; ^{1}H NMR ($CDCl_3$+DMSO-d_6, 300 MHz) δ 0.91 (t, J = 7.5 Hz, 6H), 3.13 (d, J = 15.6 Hz, 2H), 3.65-3.90 (m, 4H), 4.03 (d, J = 15.6 Hz, 2H), 6.48 (d, J = 7.5 Hz, 2H), 6.79 (t, J = 7.5 Hz, 2H), 6.95 (t, J = 7.5 Hz, 2H), 7.22 (d, J = 7.5 Hz, 2H), 9.14 (s, 2H); ^{13}C NMR ($CDCl_3$+DMSO-d_6, 150 MHz) δ 13.51, 34.05, 52.49, 60.17, 108.82, 121.16, 123.66, 127.02, 128.38, 141.45, 169.66, 178.31; ESIMS *m/z* 437 $[M+H]^+$. Anal. Calcd for $C_{24}H_{24}N_2O_6$: C, 66.04; H, 5.54; N, 6.42. Found: C, 66.37; H, 5.41; N, 6.38.

***meso*-3f:** 29%; R_f = 0.34 (CH_2Cl_2/MeOH, 19:1); white solid, mp 169-170 °C; IR (KBr) 3276, 1730, 1620, 1473, 1372 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.89 (t, J = 6.9 Hz, 6H), 3.08 (d, J = 16.2 Hz, 2H), 3.67 (d, J = 16.2 Hz, 2H), 3.60-4.00 (m, 4H), 6.50 (br s, 2H), 6.68 (d, J = 7.8 Hz, 2H), 6.78 (t, J = 7.8 Hz, 2H), 7.13 (t, J = 7.8 Hz, 2H), 7.67 (s, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 13.67, 35.87, 53.50, 60.72, 109.96, 121.56, 124.02, 127.61, 129.22, 142.37, 169.43, 177.24; ESIMS *m/z* 437 $[M+H]^+$. Anal. Calcd for $C_{24}H_{24}N_2O_6$: C, 66.04; H, 5.54; N, 6.42. Found: C, 66.20; H, 5.72; N, 6.24.

***dl*-3g:** 27%; R_f = 0.57 (hexanes/ether, 1:3); white solid, mp 253-254 °C; IR (KBr) 1713, 1611, 1470, 1376 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.95 (s, 6H), 3.63 (d, J = 14.4 Hz, 2H), 4.34 (d, J = 14.4 Hz, 2H), 5.56 (d, J = 2.7 Hz, 2H), 5.86 (app s, 2H), 6.21 (d, J = 7.5 Hz, 2H), 6.70 (t, J = 7.5 Hz, 2H), 6.85 (t, J = 7.5 Hz, 2H), 6.88 (s, 2H), 7.04 (d, J = 7.5 Hz, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 25.70, 27.91, 55.34, 107.11, 107.24, 109.75, 121.50, 123.71, 127.72, 128.18, 141.03, 143.15, 150.82, 176.91; ESIMS *m/z* 453 $[M+H]^+$.

***meso*-3g:** 24%; R_f = 0.30 (hexanes/ether, 1:3); white solid, mp 219-220 °C; IR (KBr) 1703, 1632, 1469 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.78 (s, 6H), 3.49 (d, J = 14.1 Hz, 2H), 4.09 (d, J = 14.1 Hz, 2H), 5.57 (d, J = 3.0 Hz, 2H), 5.90 (dd, J = 3.0 and 0.9 Hz, 2H), 6.49 (d, J = 7.8 Hz, 2H), 6.65 (d, J = 7.8 Hz, 2H), 6.79 (t, J = 7.8 Hz, 2H), 6.89 (d, J = 0.9 Hz, 2H), 7.12 (t, J = 7.8 Hz, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 25.83, 29.58, 56.24, 107.32, 107.72, 109.90, 121.45, 124.45, 128.08, 128.72, 141.10, 144.42, 150.30, 175.79; ESIMS *m/z* 453 $[M+H]^+$. Anal. Calcd for $C_{28}H_{24}N_2O_4$: C, 74.32; H, 5.35; N, 6.19. Found: C, 74.25; H, 5.46; N, 6.21.

***dl*-3h:** 36%; R_f = 0.47 (hexanes/ether, 1:3); white solid, mp 221-222 °C; IR (KBr) 1705, 1611, 1471, 1376 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 3.04 (s, 6H), 3.22 (dd, J = 13.2 and 8.1 Hz, 2H), 3.85 (dd, J = 13.2 and 8.1 Hz, 2H), 5.43 (dt, J = 16.2 and 8.1 Hz, 2H), 6.37 (d, J = 16.2 Hz, 2H), 6.39 (d, J = 7.5 Hz, 2H), 6.84 (t, J = 7.5 Hz, 2H), 6.94-7.22 (m, 14H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 25.67, 32.52, 56.19, 107.37, 121.78, 123.34, 124.15, 126.04, 126.92, 128.10, 128.21 (2C), 133.70, 137.39, 143.25, 176.92; ESIMS *m/z* 525 $[M+H]^+$.

***meso*-3h:** 35%; R_f = 0.19 (hexanes/ether, 1:3); white solid, mp 193-194 °C; IR (KBr) 1711, 1610, 1470, 1376 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.96 (s, 6H), 3.07 (dd, J = 12.9 and 7.8 Hz, 2H), 3.66 (dd, J = 12.9 and 7.8 Hz, 2H), 5.50 (dt, J = 15.9 and 7.8 Hz, 2H), 6.31 (d, J = 15.9 Hz, 2H), 6.66 (d, J = 7.2 Hz, 2H), 6.70 (d, J = 7.2 Hz, 2H), 6.90 (t, J = 7.2 Hz, 2H), 6.98-7.04 (m, 4H), 7.06-7.20 (m, 6H), 7.23 (t, J = 7.2 Hz, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 25.87, 34.06, 56.80, 107.93, 121.60, 123.53, 124.07, 126.04, 127.01, 128.24, 128.39, 128.68, 134.13, 137.28, 144.51, 176.04; ESIMS *m/z* 525 $[M+H]^+$. Anal. Calcd for $C_{36}H_{32}N_2O_2$: C, 82.41; H, 6.15; N, 5.34. Found: C, 82.32; H, 6.28; N, 5.19.

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